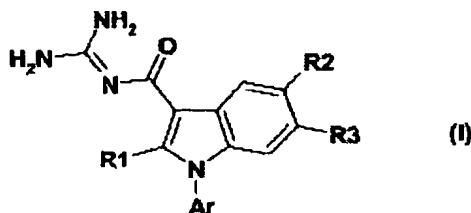


WHAT IS CLAIMED IS:

1. A compound of the formula (I)



5 wherein,

R1 is hydrogen or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms,

R2 is hydrogen or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, halogen, alkoxy having 1, 2, 3, 4, 5 or 6 carbon atoms or OH,

R3 is hydrogen or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, halogen, alkoxy having 1, 2, 3, 4, 5 or 6 carbon atoms or OH,

10 Ar is a 9- or a 10-membered bicyclic heteroaryl having one, two or three nitrogen atoms, which may be linked via any of its positions and which is substituted in at least one of its positions by alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, halogen, nitro, NRaRb, alkylcarbonylamino having 1, 2, 3 or 4 carbon atoms, hydroxyl, alkoxy having 1, 2, 3, 4, 5 or 6 carbon atoms, S(O)_nR4, CO₂H, alkoxy carbonyl having 1, 2, 3, 4, 5 or 6 carbon atoms, alkylcarbonyl having 1, 2, 3, 4, 5 or 6 carbon atoms, CONRaRb, CN, polyfluoroalkyl having 1, 2, 3 or 4 carbon atoms, polyfluoroalkoxy having 1, 2 or 3 carbon atoms or SO₃H,

15 n = 0, 1 or 2,

20 Ra and Rb

are independently of each other hydrogen, linear or branched alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms or Ra and Rb form, together with the nitrogen atom to which they are attached, a 5- or 6-membered heterocycle, which may optionally contain another hetero atom chosen from O, S and N,

25 R4 is alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, alkylamino having 1, 2, 3, 4, 5 or 6 carbon atoms or NH₂,

or a racemic mixture, enantiomer, diastereomer, or tautomer of such compound, or a mixture thereof, or a pharmaceutically acceptable salt of such compound, racemic mixture, enantiomer, diastereomer, tautomer, or mixture.

5 2. A compound according to claim 1 wherein:

R1 is hydrogen or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms,

R2 is hydrogen or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, halogen, alkoxy having 1, 2, 3, 4, 5 or 6 carbon atoms or OH,

R3 is hydrogen or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, halogen, alkoxy having 1, 2, 3, 4, 5 or 6 carbon atoms or OH,

10 Ar is quinoline, isoquinoline, quinazoline or 7H-pyrrolo-[2,3-d]-pyrimidine, which may be linked via any of its positions and which is substituted in at least one of its positions by alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, halogen, nitro, NRaRb, alkylcarbonylamino having 1, 2, 3 or 4 carbon atoms, hydroxyl, alkoxy having 1, 2, 3, 4, 5 or 6 carbon atoms, S(O)_nR4, CO₂H, alkoxycarbonyl having 1, 2, 3, 4, 5 or 6 carbon atoms, alkylcarbonyl having 1, 2, 3, 4, 5 or 6 carbon atoms, CONRaRb, CN, polyfluoroalkyl having 1, 2, 3 or 4 carbon atoms, polyfluoroalkoxy having 1, 2 or 3 carbon atoms or SO₃H,

15 n = 0, 1 or 2,

20 Ra and Rb are independently of each other hydrogen, linear or branched alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms or Ra and Rb form, together with the nitrogen atom to which they are attached, a 5- or 6-membered heterocycle, which may optionally contain another hetero atom chosen from O, S and N,

25 R4 is alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, alkylamino having 1, 2, 3, 4, 5 or 6 carbon atoms or NH₂.

3. A compound according to claim 1 wherein:

R1 is hydrogen or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms,

R2 is hydrogen or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, halogen, alkoxy having 1, 2, 3, 4, 5 or 6 carbon atoms or OH,

R3 is hydrogen or alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, halogen, alkoxy having 1, 2, 3, 4, 5 or 6 carbon atoms or OH,

Ar is 4-quinolinyl, 4-quinazolinyl or 4-(7H-pyrrolo-[2,3-d]-pyrimidinyl), which is substituted in at least one of its positions by alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, halogen, nitro, NR_aR_b, alkylcarbonylamino having 1, 2, 3 or 4 carbon atoms, hydroxyl, alkoxy having 1, 2, 3, 4, 5 or 6 carbon atoms, S(O)_nR₄, CO₂H, alkoxy carbonyl having 1, 2, 3, 4, 5 or 6 carbon atoms, alkylcarbonyl having 1, 2, 3, 4, 5 or 6 carbon atoms, CONR_aR_b, CN, polyfluoroalkyl having 1, 2, 3 or 4 carbon atoms, polyfluoroalkoxy having 1, 2 or 3 carbon atoms or SO₃H,

5 n = 0, 1 or 2,

R_a and R_b

are independent of each other hydrogen, linear or branched alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms or R_a and R_b form, together with the nitrogen atom to which they are attached, a 5- or 6-membered heterocycle, which may optionally

15 contain another hetero atom chosen from O, S and N,

R4 is alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, alkylamino having 1, 2, 3, 4, 5 or 6 carbon atoms or NH₂.

4. A compound according to claim 1 which is

20 3-Guanidinocarbonyl-1-(2-(trifluoromethyl)quinol-4-yl)-1H-indole,

3-Guanidinocarbonyl-1-(6-(trifluoromethyl)quinol-4-yl)-1H-indole,

3-Guanidinocarbonyl-1-(7-(trifluoromethyl)quinol-4-yl)-1H-indole,

3-Guanidinocarbonyl-1-(8-(trifluoromethyl)quinol-4-yl)-1H-indole,

3-Guanidinocarbonyl-1-(6-methoxyquinol-4-yl)-1H-indole,

25 3-Guanidinocarbonyl-1-(7-methoxyquinol-4-yl)-1H-indole,

3-Guanidinocarbonyl-1-(2-methylquinol-4-yl)-1H-indole,

3-Guanidinocarbonyl-1-(6-chloroquinol-4-yl)-1H-indole,

3-Guanidinocarbonyl-1-(7-chloroquinol-4-yl)-1H-indole,

3-Guanidinocarbonyl-1-(8-chloroquinol-4-yl)-1H-indole,

30 3-Guanidinocarbonyl-1-(6-fluoroquinol-4-yl)-1H-indole,

3-Guanidinocarbonyl-1-(8-fluoroquinol-4-yl)-1H-indole,

3-Guanidinocarbonyl-1-(6,8-difluoroquinol-4-yl)-1H-indole,

3-Guanidinocarbonyl-1-(6-fluoro-2-methylquinol-4-yl)-1H-indole,
3-Guanidinocarbonyl-1-(7-fluoro-2-methylquinol-4-yl)-1H-indole,
3-Guanidinocarbonyl-1-(8-fluoro-2-methylquinol-4-yl)-1H-indole,
3-Guanidinocarbonyl-1-(7-methyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-indole,

5 3-Guanidinocarbonyl-1-(7-chloroquinol-4-yl)-5-methoxy-2-methyl-1H-indole,
3-Guanidinocarbonyl-1-(6-fluoroquinol-4-yl)-5-methoxy-2-methyl-1H-indole,
or
3-Guanidinocarbonyl-1-(6-chloro-quinazolin-4-yl)-5-methoxy-2-methyl-1H-indole,
or a tautomer thereof or a pharmaceutically acceptable salt of such compound or
10 tautomer.

5. A pharmaceutical composition for human, veterinary, or phytoprotective use comprising a pharmaceutically effective amount of a compound according to claim 1 together with a pharmaceutically acceptable medium.

15 6. A pharmaceutical composition for human, veterinary, or phytoprotective use comprising a pharmaceutically effective amount of a compound according to claim 1 together with a pharmaceutically acceptable medium in combination with a pharmaceutically effective amount of another pharmacologically active ingredient or
20 medicament.

7. A method for the treatment or prophylaxis of cardiovascular disease, metabolic disease, cancerous disease, or fibrotic disease comprising administering to a patient in need thereof, a pharmaceutically effective amount of a compound according to claim 1.

25 8. A method for the treatment or prophylaxis of acute or chronic damage to, or disorders or indirect sequelae of organs and tissues caused by ischemic or reperfusion events;
arrhythmias, life-threatening cardiac ventricular fibrillation, myocardial
30 infarction, angina pectoris;

ischemic states of the heart, ischemic states of the peripheral and central nervous system, stroke, cerebral oedema attack, ischemic states of peripheral organs and tissues;

states of shock;

5 diseases in which cellular proliferation represents a primary or secondary cause;

cancer, metastasis, prostate hypertrophy, prostate hyperplasia;

atherosclerosis, disturbances of lipid metabolism, high blood pressure;

disorders of the central nervous system;

10 non-insulin-dependent diabetes mellitus, late damage from diabetes; thromboses, disorders resulting from endothelial dysfunction, intermittent claudication;

fibrotic disorders of internal organs, fibrotic disorders of the liver, fibrotic disorders of the kidney, fibrotic disorders of vessels, fibrotic disorders of lung, fibrotic

15 disorders of the heart;

heart failure, congestive heart failure, acute or chronic inflammatory disorders, disorders caused by protozoa;

malaria, or coccidiosis in poultry, comprising administering to a patient in need thereof, a pharmaceutically effective amount of a compound according to claim 1.

20

9. A method according to claim 8 for the treatment or prophylaxis of allergic shock, cardiogenic shock, hypovolaemic shock or bacterial shock.

25 10. A method according to claim 8 for the treatment or prophylaxis of essential hypertension.

11. A method according to claim 8 for the treatment or prophylaxis of disorders resulting from overexcitability of the CNS.

30 12. A method according to claim 11, for the treatment or prophylaxis of epilepsy or centrally induced convulsions.

13. A method according to claim 8 for the treatment or prophylaxis of anxiety states, depressions or psychoses.

14. A method for protecting an organ in a transplant donor during organ
5 transplantation, both before and during the removal of the organ, comprising
administering to said donor, a pharmaceutically effective amount of a compound
according to claim 1.

15. A method for protecting a removed organ during treatment with, or storage in
10 physiological bath liquids, comprising contacting said organ with a compound
according to claim 1.

16. A method for protecting a removed organ during transfer to a recipient organism
during organ transplantation, comprising contacting said organ with a compound
15 according to claim 1.

17. A method for preventing age-related tissue change, in a patient in need thereof,
comprising administering to said patient, a pharmaceutically effective amount of a
compound according to claim 1.

20 18. A method for prolonging life in a patient in need thereof, comprising
administering to said patient, a pharmaceutically effective amount of a compound
according to claim 1.

25 19. A method for the treatment or reduction of the cardiotoxic effects in
thyrotoxicosis in a patient in need thereof, comprising administering to said patient a
pharmaceutically effective amount of a compound according to claim 1.

20. A diagnostic agent comprising a compound according to claim 1.

30 21. A method for the treatment or prophylaxis of

acute or chronic damage to, or disorders or indirect sequelae of organs and tissues caused by ischemic or reperfusion events;

arrhythmias, life-threatening cardiac ventricular fibrillation, myocardial infarction, angina pectoris;

5 ischemic states of the heart, ischemic states of the peripheral and central nervous system, stroke, cerebral oedema attack, ischemic states of peripheral organs and tissues;

states of shock;

10 diseases in which cellular proliferation represents a primary or secondary cause;

cancer, metastasis, prostate hypertrophy, prostate hyperplasia;

atherosclerosis, disturbances of lipid metabolism, high blood pressure;

disorders of the central nervous system;

non-insulin-dependent diabetes mellitus, late damage from diabetes;

15 thromboses, disorders resulting from endothelial dysfunction, intermittent claudication;

fibrotic disorders of internal organs, fibrotic disorders of the liver, fibrotic disorders of the kidney, fibrotic disorders of vessels, fibrotic disorders of lung, fibrotic disorders of the heart;

20 heart failure, congestive heart failure, acute or chronic inflammatory disorders, disorders caused by protozoa;

malaria, or coccidiosis in poultry, comprising administering to a patient in need thereof, a pharmaceutically effective amount of a compound according to claim 1, in combination with a pharmaceutically effective amount of another medicament or active ingredient.

22. A method according to claim 21 for the treatment or prophylaxis of allergic shock, cardiogenic shock, hypovolaemic shock or bacterial shock.

30 23. A method according to claim 21 for the treatment or prophylaxis of essential hypertension.

24. A method according to claim 21 for the treatment or prophylaxis of disorders resulting from overexcitability of the CNS.

25. A method according to claim 24, for the treatment or prophylaxis of epilepsy or centrally induced convulsions.

26. A method according to claim 21 for the treatment or prophylaxis of anxiety states, depressions or psychoses.

10 27. A method for protecting an organ in a transplant donor during organ transplantation, both before and during the removal of the organ, comprising administering to said donor, a pharmaceutically effective amount of a compound according to claim 1 in combination with a pharmaceutically effective amount of another medicament or active ingredient.

15 28. A method for protecting a removed organ during treatment with, or storage in physiological bath liquids, comprising contacting said organ with a compound according to claim 1 in combination with another medicament or active ingredient.

20 29. A method for protecting a removed organ during transfer to a recipient organism during organ transplantation, comprising contacting said organ with a compound according to claim 1 in combination with another medicament or active ingredient.

25 30. A method for preventing age-related tissue change, in a patient in need thereof, comprising administering to said patient, a pharmaceutically effective amount of a compound according to claim 1 in combination with a pharmaceutically effective amount of another medicament or active ingredient.

30 31. A method for prolonging life in a patient in need thereof, comprising administering to said patient, a pharmaceutically effective amount of a compound according to claim 1 in combination with a pharmaceutically effective amount of another medicament or active ingredient.

32. A method for the treatment or reduction of the cardiotoxic effects in thyrotoxicosis in a patient in need thereof, comprising administering to said patient a pharmaceutically effective amount of a compound according to claim 1 in combination

5 with a pharmaceutically effective amount of another medicament or active ingredient.

33. A diagnostic agent comprising a compound according to claim 1 in combination with an another medicament or active ingredient.

10 34. A method of reducing the cardiotoxic or cytotoxic effects of cardiotoxic or cytotoxic medicaments or active ingredients having cardiotoxic or cytotoxic properties, in a patient in need thereof, comprising administering to said patient, a pharmaceutically effective amount of a compound according to claim 1 in combination with a pharmaceutically effective amount of said cardiotoxic or cytotoxic medicament

15 or active ingredient.

35. A method for the treatment or prophylaxis of acute or chronic damage, disorders or indirect sequelae of organs or tissues caused by ischemic or reperfusion events in a patient in need thereof, comprising administering to said patient a pharmaceutically

20 effective amount of a compound according to claim 1.

36. A method for the treatment or prophylaxis of acute or chronic damage, disorders or indirect sequelae of organs or tissues caused by ischemic or reperfusion events in a patient in need thereof, comprising administering to said patient a

25 pharmaceutically effective amount of a compound according to claim 1 in combination with a pharmaceutically effective amount of another medicament or active ingredient.

37. A method for the treatment of life-threatening cardiac ventricular fibrillation, in a patient in need thereof, comprising comprising administering to said patient, a

30 pharmaceutically effective amount of a compound according to claim 1.

38. A method for the treatment of life-threatening cardiac ventricular fibrillation, in a patient in need thereof, comprising administering to said patient, a pharmaceutically effective amount of a compound according to claim 1 in combination with a pharmaceutically effective amount of another medicament or active ingredient.

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39. A method for the treatment or prophylaxis of metastasis in a patient in need thereof, comprising administering to said patient a pharmaceutically effective amount of a compound according to claim 1.

10 40. A method for the treatment or prophylaxis of metastasis in a patient in need thereof, comprising administering to said patient a pharmaceutically effective amount of a compound according to claim 1 in combination with a pharmaceutically effective amount of another medicament or active ingredient.

15 41. A method for the treatment or prophylaxis of fibrotic disorders of the heart, heart failure, or congestive heart failure, in a patient in need thereof, comprising administering to said patient a pharmaceutically effective amount of a compound according to claim 1.

20 42. A method for the treatment or prophylaxis of fibrotic disorders of the heart, heart failure, or congestive heart failure, in a patient in need thereof, comprising administering to said patient a pharmaceutically effective amount of a compound according to claim 1 in combination with a pharmaceutically effective amount of another medicament or active ingredient.

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43. A method for the treatment or prophylaxis of a disease which is related to NHE, in a patient in need thereof, comprising administering to said patient a pharmaceutically effective amount of a compound according to claim 1.

30 44. A method for the treatment or prophylaxis of a disease which is related to NHE, in a patient in need thereof, comprising administering to said patient a

pharmaceutically effective amount of a compound according to claim 1 in combination with an effective amount of another medicament or active ingredient.

45. A method for the treatment or prophylaxis of a disease which is related to

5 NHE1, in a patient in need thereof, comprising administering to said patient a pharmaceutically effective amount of a compound according to claim 1.

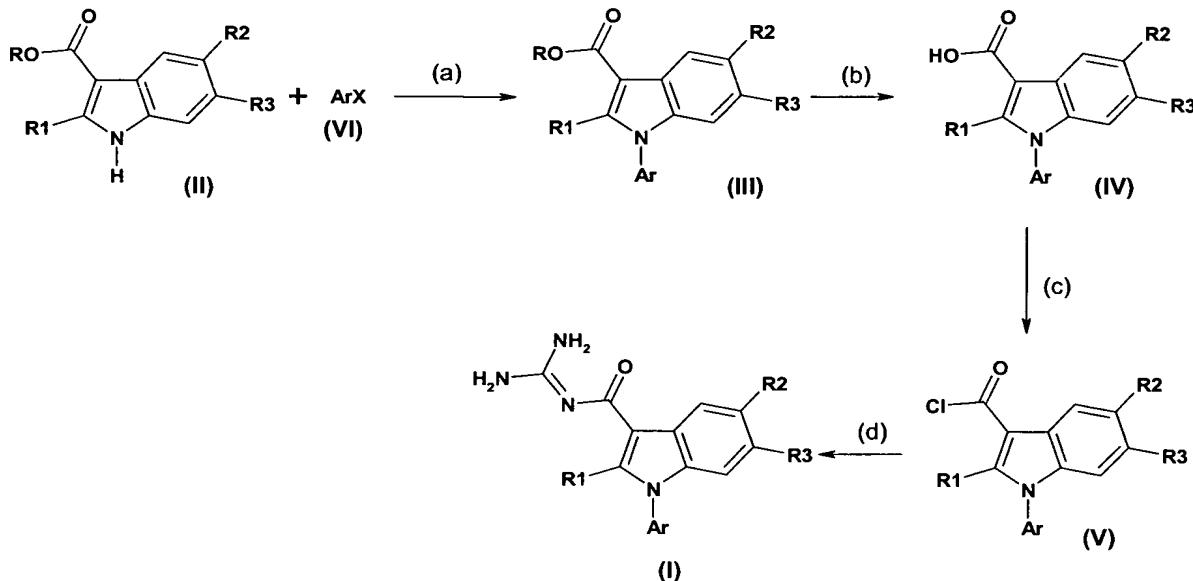
46. A method for the treatment or prophylaxis of a disease which is related to NHE1, in a patient in need thereof, comprising administering to said patient a

10 pharmaceutically effective amount of a compound according to claim 1 in combination with a pharmaceutically effective amount of another medicament or active ingredient.

47. A method for protecting the organs or blood vessels during surgical intervention, in a patient in need thereof, comprising administering to such patient a

15 pharmaceutically effective amount of a compound according to claim 1.

48. A process for the preparation of a compound according to claim 1, comprising



a) reacting a heteroaryl halide ArX of the formula (VI) with a 3-alkoxycarbonyl-1H-

20 indole of the formula (II);

b) saponifying the obtained 3-alkoxycarbonyl-1-heteroaryl-indole of the formula (III);

c) converting the obtained 3-carboxy-1-heteroaryl-indole of the formula (IV) to the corresponding acid chloride of the formula (V);

d) reacting the acid chloride of formula (V) with guanidine, and isolating the compound according to claim 1; and optionally converting it into a

5 pharmaceutically acceptable salt thereof,

wherein in the compounds of the formula II, III, IV, V and VI

Ar and R1 to R3 are defined as in claim 1,

X is F, Cl, Br or I and

R is alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms.